miums to his credit. Let, therefore, the charitable maxim of Sir Charles Bell ever be kept in view.

"He who makes the philosophy of the human system his study, must be taught humility, and learn from his own errors how to look kindly on others."

ART. II.—*On the Modus Operandi of Medicines.* By JOHN B. BECK, M. D., Prof. of Materia Medica and Medical Jurisprudence, in the College of Physicians and Surgeons of New York.

THERE is perhaps no subject which has attracted more attention than the modus operandi (as it is commonly called) of medicines, or the manner in which the effects of medicines are produced upon the living system. It is by no means singular that it should have been so. It is a subject, not merely interesting as a matter of theoretical speculation, but one involving results of great practical importance. As may naturally be supposed, the most opposite opinions have been entertained in relation to it, and even at the present time, there is a wide difference in the doctrines and belief of eminent men on the subject. It is not my intention to enter into the full discussion of it, on the present occasion. After some general observations, the main object which I have in view, is to bring forward a summary of the facts which go to establish one principal point connected with it, and that is the absorption of medicines into the circulation.

The effects of medicines are divided into those which are *local*, and those which are *remote*. By the first, are meant those impressions which a medicine makes upon the part with which it comes in immediate contact. By the second, are meant those which show themselves in distant parts of the system.

Now with regard to the first of these, our knowledge is confined to very narrow limits. All that we can say about it is, that the medicine, whatever it may be, comes in actual contact with a living surface and produces upon it peculiar effects, corresponding to the nature of the substance applied, and the particular susceptibility of the part to which it is applied. In short, our knowledge does not extend beyond the simple expression of the fact itself. *How* it is, or *why* it is, that such effects are produced, are subjects entirely beyond our comprehension.

With regard to the *remote* effects, the question which presents itself is of a different character. In what way is it that medicines when locally applied are capable of producing effects upon distant parts of the system? How is it that agents taken into the stomach, or applied to the skin, can affect the brain, the lungs, the kidneys, the uterus, &c.? This is a question by no means of easy solution, and has been greatly embarrassed by the theories and speculations of ingenious men. In discussing it, I shall endeavour to keep aloof from

these theories, and confine myself to such views as may be sustained by fact as well as argument.

There are only two ways in which different parts of the system can hold intercourse or be acted upon by one another. The first of these is through the medium of the *nerves*—the second, through the medium of the *circulation.* It is only in one or other of these ways therefore, that the effects of medicinal agents can be produced in distant parts of the system. In other words, the impression made by the medicine upon the part to which it is applied must be conveyed sympathetically to other parts, or the medicine must be taken into the circulation, and actually carried to different parts of the system, and thus produce its remote effects. A candid review of all the facts connected with the subject will lead us, I think, to the conclusion, that in neither of these modes exclusively are the remote effects of medicines produced, but that while in some cases they are produced by sympathy, in others they are the result of absorption into the circulation: and these are the points which I shall endeavour to establish.

In the first place, *of the production of the remote effects by sympathy.* The human system is so constituted that no part of it is completely isolated from the rest. Impressions made upon one portion of it, are extended with different degrees of force to other portions. An incessant intercourse is thus kept up throughout the complicated machinery of the animal economy, and the agents through which this is accomplished are the nerves ramifying through every fibre of the system. Now that medicinal, like other impressions, are propagated from one part of the body to another in this way, is unquestionable, and the great fact which, independently of other considerations, proves this beyond a doubt, is the *rapidity* with which the remote effects are in many cases developed. Thus, for example, ammonia held to the nostrils, almost immediately rouses from a fit of fainting. A person in a state of lassitude and fatigue may have his spirits exhilarated, and tone given to his whole system at once by a small quantity of wine. In some cases of vertigo, the head is frequently relieved almost instantaneously by a teaspoonful of ether in a glass of water. Now, in these cases, as well as many others which might be adduced, the effect is too speedy to be produced in any other way than through nervous or sympathetic agency.

Experiments made upon animals with certain poisonous agents show this in a still more conclusive manner. By Majendie, the extremity of a glass tube previously dipped into a phial containing pure prussic acid, was plunged into the throat of a strong dog. The tube had scarcely come in contact with the tongue, before the animal made two or three long and rapid inspirations and fell dead. No method that could be devised, enabled him to trace the smallest sign of sensibility in the muscular organs of this animal after death.

An atom of the acid was applied to the eye of another dog—the effects were as sudden and as fatal as in the preceding experiment.

A drop of the acid diluted with four drops of alcohol were injected into

the jugular vein of a third dog. The animal fell dead that instant, as if struck by a cannon shot or by lightning.*

By Mr. Brodie, two ounces of proof spirit were introduced into the stomach of a rabbit, and produced perfect insensibility almost before the injection was completed.

One drop of the essential oil of bitter almonds, applied to the tongue of a cat, caused instant convulsions.

Three ounces of the infusion of tobacco, injected into the rectum of a dog, produced immediate contractions of the voluntary muscles.

Less than a drop of the empyreumatic oil of tobacco, applied to the tongue of a young cat, caused instant convulsions.†

By Dr. Christison, a dog was killed in less than three seconds, by introducing into the left femoral vein two drops of conia, neutralized with muriatic acid, and diluted with thirty drops of water.‡

The foregoing illustrations are sufficient to show the rapidity with which impressions may be conveyed from one part of the system to another—a fact inexplicable, except upon the supposition of their being transmitted through the nerves.

In the second place, *of the production of the remote effects by the absorption of medicines into the circulation.*—In the investigation of this point, two things require to be noticed; 1. are medicines actually absorbed, and 2. are the remote effects the result of this absorption.

Strange as it may appear, notwithstanding the multiplied proofs to the contrary, it has been actually denied, and that by writers of authority too, that medicines are ever taken into the circulation, and the most elaborate and ingenious efforts have been made to establish this doctrine.

In every discussion it is essential to settle two preliminary points, and these are, what the question precisely at issue is, and then what the kind of evidence is which is necessary to establish or refute it. In the present case the question at issue is this—do or do not certain medicines enter the circulation? and the kind of evidence necessary to determine it must be that of fact and experiment. This is the only kind of evidence which can settle it. General reasonings can do nothing more than show the probability, or improbability of it. Further than this they cannot go, and therefore as opposed to actual fact, they can be accounted of no moment. I make these observations, because some of the writers to whom I have alluded, in their discussions of this subject, overlooking the evidence of facts, appear to me to have trusted almost entirely to general speculations, a species of argumentation altogether inapplicable. To settle this question, then, all that we have to do is to ascertain from actual observation and

* Brande's Journal of Arts and Sciences, vol. 4, p. 348.

† Eclectic Repertory, vol. 2, p. 270.

‡ On the Poisonous properties of Hemlock and its alkaloid, conia. By R. Christison, M. D. From the Transactions of the Royal Society of Edinburgh, p. 33.

experiment, whether or not, substances introduced into the alimentary canal or applied to the surface, can afterwards be detected in the fluids or solids of the system. It is altogether a question of fact, not of argument. Let us then see what is the evidence furnished by well attested facts in relation to this subject.

Of the Chyle.—Of the presence of foreign substances in the chyle, we have several striking proofs. Into the jejunum of a dog who had been kept fasting for a day previous, Dr. Musgrave injected twelve ounces of a *solution of indigo* in fountain water. After three hours, the dog was opened again, when several of the lacteals were observed of a bluish colour, showing the presence of the indigo in these vessels. Another experiment of a similar kind was made by him, by injecting *blue stone* in solution into the jejunum of a dog, that had been kept fasting thirty-six hours. In a few minutes after the injection, the lacteals became of a perfectly blue colour. Another experiment was made upon a spaniel that had been kept fasting thirty-six hours, by injecting with a syringe into one of the small intestines a pint of a deep decoction of *blue stone* with water. After three hours, the dog was again opened, when the lacteals were found of a deep blue colour. That there might be no mistake about it, several of the lacteals were cut, and a blue liquor was poured out running down on the mesentery. The thoracic duct was now examined and the same appearances observed.*

By Dr. Fordyce, a solution of *indigo* was injected into the intestines of a sheep, and the chyle afterwards found quite blue.†

By Tiedemann and Gmelin, *sulphate of iron* was detected in the chyle of a horse who had taken it. *Prussiate of potass* was found in the chyle of a dog, and *sulphuro-prussiate of potash* in the chyle of another dog to whom it had been given.‡

By Dr. Milnor of Philadelphia, a cat was fed for several days on *Prussian blue and indigo.* At the expiration of thirteen days it was killed, and on examining the chyle it was found tinged with blue, so as to be easily distinguishable from natural chyle.§ A dog was also fed for several days on *madder*, and afterwards on *anotta.* After death, on examination, the chyle of the thoracic duct was found "tinged with the article given."‖ Another dog was fed on *indigo* for ten days, and on dissection the mesenteric lacteals were found distended with chyle of a light bluish tinge.¶

By the late Dr. Macnevin, Professor of Chemistry in the College of Physicians and Surgeons of New York, the following experiment was made:—One drachm of *hydrocyanate of potassa*, triturated and mixed with bread and butter, was given to a dog. Between three and four hours after, he was killed by giving him hydrocyanic acid. The lacteals and thoracic duct

* Philosophical Transactions of London—Percival's Essays. Vol. 2, p. 317.

† A Treatise on the digestion of food. By G. Fordyce, M. D. &c. Lond. 1791, p. 122.

‡ Philadelphia Journal of Medical and Physical Sciences, vol. 3. p. 153.

§ Ibid. vol. 4, p. 14. ‖ Ibid. p. 16. ¶ Ibid. p. 17.

were soon filled with milk-white chyle. On scratching the receptaculum and pressing down the duct, nearly half a tea-spoonful of chyle was collected. Into this was let fall a couple of drops of the solution of permuriate of iron, and a deep blue was the immediate consequence.*

By Drs. Coates, Lawrence and Harlan, experiments were made upon several animals by giving them the *ferrocyanate of potass*, and on testing the chyle afterwards with sulphate of iron it struck a deep blue, showing the presence of it in this fluid.† By the same persons the *green sulphate of iron* was injected into the abdomen of three different kittens, and on testing the chyle with prussiate of potass, it struck a deep blue in all three.‡ An ounce of *tincture of assafœtida* was injected by them, into the abdomen of a cat, and on opening the animal, the chyle in the thoracic duct emitted the peculiar odour of that article.§

The foregoing facts appear to me sufficient to show that foreign substances may and do actually, sometimes at least, get into the chyle and in that way pass into the circulation. That this is the usual route, however, which they take would seem to be disproved by numerous experiments. This has been shown particularly to be the case with coloured substances. By Tiedemann and Gmelin, indigo, sap green, gamboge, madder, rhubarb, alkanet and tincture of litmus were given to animals, and in none could they afterwards be detected in the chyle either of the lacteals or of the thoracic duct, although they were discovered in the blood and the urine. Majendie could not detect in the chyle of dogs, indigo, rhubarb, madder or saffron which had been given to them. By Lawrence and Coates too, in their experiments no change of colour could be detected in the chyle. As the result therefore of all the experiments with regard to colouring matters, it would appear that although occasionally they may get into the chyle, yet as a general rule, when they pass into the circulation they do so through another route, and that is through the absorbing veins.‖ With regard to certain saline substances, however, the case is different. Prussiate of potash, the article generally used in the foregoing experiments, not merely enters the chyle, but does so with great facility. In experiments made by Lawrence and Coates upon thirty-four animals, sixteen indicated the presence of this salt in the chyle.¶

* New York Medical and Physical Journal, vol. 1, p. 131.

† Account of Experiments to determine the absorbing powers of the veins and lymphatics. Phil. Journal of Medical and Physical Sciences, vol. 3, pp. 293, 4, 5, 6. Vol. 5, pp 329, 30, 31.

‡ Ibid. vol. 5, p. 342. § Ibid. vol. 3, p. 291.

‖ It is to be recollected that none of the experimentalists, mentioned above, express any doubt at all of the entrance of foreign substances into the circulation—the only question being, whether they enter it through the medium of the lacteals and thoracic duct or through the medium of the veins; a question, which, however interesting in itself, has no important bearing on the present discussion. For an excellent view of this latter subject I may refer to Dunglison's Physiology, vol. 2.

¶ Phil. Journal of Medical and Physical Sciences, vol. 5, p. 328.

Of the Blood.—That foreign substances taken into the stomach are afterwards found in the blood, is still better established than their presence in the chyle. On this point the experiments are numerous and unequivocal. By Tiedemann and Gmelin, in their experiments upon animals, the following substances were detected in the blood of the *mesenteric veins*, viz: camphor, musk, indigo, rhubarb, prussiate of potass, sulphate of potash, traces of lead and iron. In the blood of the *splenic veins*, they detected musk, alcohol, rhubarb, prussiate of potash, traces of lead, iron, and of mercury. In the blood of the *vena portæ*, they detected camphor, Dippel's animal oil, musk, rhubarb, prussiate of potash, sulphuro-prussiate of potash, iron, lead and barytes.*

By experimenters in our own country, similar facts have been established. By Dr. Milnor, the odour of *musk* was detected in the blood of the vena portæ of a dog to whom it had been previously given. He also found the smell of *garlic* in the blood drawn from the jugular vein of a dog fed upon it.† By Prof. Macnevin, the hydro-cyanate of potassa was detected in the serum of the blood of the vena portæ of a dog to whom it had been given.‡ By Drs. Coates, Lawrence and Harlan, the same substance, introduced into the stomachs of animals, was in numerous experiments, discovered in the blood of the heart, the aorta and the vena portæ.§

Still more recently, the celebrated Orfila has established the fact that *arsenic, antimony and the salts of copper* may be detected in the blood of animals poisoned by these metals.‖ With regard to arsenic too, he has shown that the same may be done in cases of poisoning by this article in the human subject. In a case, in which the patient recovered after swallowing nearly a tea-spoonful of arsenious acid, the presence of the metal was detected in the blood which had been drawn from the arm for the purpose of relieving the inflammatory symptoms.¶

The foregoing facts are decisive to show that foreign substances taken into the stomach do afterwards pass into the blood. The proof which they furnish is so plain and positive, that one could hardly suppose any but the most visionary theorist capable of undertaking to evade it. The only objection that can be urged, is that most of the experiments were made upon animals, and therefore that it can only be inferred analogically that similar effects would take place in the human subject. This, however, will scarcely be urged. If it should, the facts which we have to show the presence of foreign substances in the secretions, not merely in animals

* Recherches sur la route que prennent diverses substances pour passer de l'estomac et du canal intestinal dans le sang, &c. Par. E. Tiedemann et Gmelin. Traduit par S. Heller, p. 64, &c.

† Philadelphia Journal of Medical and Physical Sciences, vol. 4, pp. 16, 18.

‡ New York Medical and Physical Journal, vol. 1, p. 132.

§ Philadelphia Journal of Medical and Physical Sciences, vol. 5, p. 329.

‖ Johnson's Journal, vol. 38, p. 429.

¶ Ibid., vol. 38, p. 430.

but in man, will do away entirely with this objection. These we next proceed to state.

Of the Urine.—Every body knows from common observation, the effect of certain articles on the urine. Asparagus gives it a well known and peculiar smell. Turpentine gives it a violet odour. Juniper berries are said to do the same. According to John, the urine of those who have taken valerian, has a smell like that of myrrh—and he asserts that castor, assafœtida and saffron communicate their peculiar odour to the urine.* By Sir Everard Home, *rhubarb* was detected in the urine of several animals, to whom it had been previously given both in the form of tincture and infusion. The test used was the caustic alkali, originally suggested by Mr. Brande.† By Dr. Milnor, the same substance was found in the urine of two dogs who had been fed upon it.‡ By Dr. Macnevin, the *hydrocyanate of potassa* was detected in the urine of a dog,§ and the same was done in numerous experiments on animals by Drs. Lawrence and Coates.‖ By the same persons, the *green sulphate of iron*, injected into the abdomen of a kitten, was afterwards detected in the urine.¶ One of the substances which enters the urine with the greatest facility, and indeed all the other fluids of the system, is *iodine*. Dr. O'Shaughnessy found it in the urine of a dog poisoned with it, in forty minutes after taking it.** Lugol states that in some cases, it was found in the urine of patients using it, almost immediately after the dose was taken.†† Dr. Rees, of London, detected it in the urine of a person who had taken only one Thomson, it has also been detected in the urine of persons using it.§§ By grain, in three separate doses of a third of a grain each.‡‡ By Dr. A. T. Dr. Cogswell, experiments were made upon eleven individuals, by giving them iodine in various forms, viz: the *tincture*—solution of *iodide of potassium* and *iodide of iron* in solution, and in the urine of ten of them, the presence of iodine was distinctly ascertained.‖‖

Iodine has also been detected in the urine in consequence of the external application of it. This was satisfactorily proved by Dr. Madden in five different experiments, by immersing his arm in a tepid solution of iodide of potassium, and afterwards testing the urine.¶¶

* New York Medical and Physical Journal, vol. 5, p. 624.

† On the Structure and Uses of the Spleen. By E. Home, Esq. F. R. S. Philosophical Transactions of the Royal Society for 1808, pp. 45, 133.

‡ Philadelphia Journal of Medical and Physical Sciences, vol. 4, pp. 16, 18.

§ New York Medical and Physical Journal, vol. 1, p. 131.

‖ Philadelphia Journal of Medical and Physical Sciences, vol. 5, p. 329.

¶ Ibid., vol. 5, p. 368.

** London Lancet for March 26, 1836, p. 6.

†† Essays on the Effects of Iodine, &c. p. 20.

‡‡ On the Analysis of the Blood and Urine. By G. O. Rees, p. 88.

§§ Johnson's Medico-Chirurgical Journal, vol. 29, p. 215.

‖‖ An Experimental Essay, &c. on Iodine and its Compounds. By Charles Cogswell, A. B., M. D., &c. *Ed.* p. 57.

¶¶ An Experimental Inquiry into the Physiology of Cutaneous Absorption, &c. By Wm. H. Madden, M. D., p. 103.

By Cantu, globules of *quicksilver* were obtained from the urine of persons under the action of mercurials*—and on the authority of Prof. E. D. Smith, of South Carolina, it is stated that M. L'Herminier, a French chemist, found the *phosphate of mercury* in the urine of a child, that had been taking calomel internally for some time previously.†

By M. Piorry, the *sulphate of quinia* was detected in the urine of patients under its use.‡

Tannin, which exists in a great number of vegetable matters used as remedial agents, is frequently found in the urine. In this case the fluid strikes a dark colour with the persalts of iron.§

Among the most curious facts, however, that we have on this subject are those reported by Stehberger. These are a series of experiments made by him, under the superintendence of Tiedemann. The subject was a young man, thirteen years of age, who was affected with congenital prolapsus of the bladder. The prolapsus formed at the lower part of the abdomen, a projection of three fingers breadth, which was red and fungous, always moist and sensible to the touch. The urine issued continually from the ureters, which were completely exposed, and admitted of the secretion of the kidneys being collected perfectly pure and unmixed. When any substance had been administered, the urine was collected every ten minutes, until indications of it were perceived. It was then examined every quarter or half hour, until the urine had returned to its original character. In this manner the progressive augmentation and diminution of the foreign substance was observed. The period which elapsed between the swallowing of the different articles and their appearance in the urine was as follows: Madder was perceptible in 15 minutes—indigo, in 15—rhubarb, in 20—gallic acid, in 20—decoction of logwood, in 25—the colouring principle of myrtle berries, in 30—black cherries, in 45—the astringent principle of uva ursi, in 45—the pulp of cassia, in 55—prussiate of iron, in 60—rob of elder, in 75. The complete disappearance of the substances from the urine was as follows: Prussiate of iron, in three hours and three quarters—indigo, four hours and a half—rhubarb, six hours and twenty minutes—decoction of logwood, in six hours and three quarters—uva ursi, seven hours and twenty minutes—myrtle berries, eight hours and three quarters—madder, nine hours—gallic acid, eleven hours—pulp of cassia, twenty-four hours.‖ These experiments are eminently interesting, not merely as establishing the general fact that foreign substances do get into the urine, but as showing the rapidity with which some of them get there, as well as the length of time which they continue to pervade that fluid.

* New York Medical and Physical Journal, vol. 5, p. 381. Also, Christison on Poisons, p. 292.

† American Journal of Science and Arts. By B. Silliman, M. D. &c., vol. 3, p. 306.

‡ Johnson's Journal, vol. 29, p. 215.

§ Rees on the Blood and Urine, p. 88.

‖ New York Medical and Physical Journal, vol. 6, p. 130.

By Wohler, a still more extensive series of experiments are reported, the object of which was to show, not merely that foreign substances pass off by the urine, but in addition to this, to point out the changes which they undergo in their passage through the system. The results, as stated by him, are that some pass off by the urine decomposed—others in a state of new combination—while a third pass off unchanged. Those which are *decomposed* are the following: the tartrates, citrates, malates and acetates of potash and soda, changed into carbonates of the same alkalies. Hydro-sulphuret of potash, changed into the sulphate of potash. Those which enter into *new combinations* with substances which they find in the body are the following: sulphur, changed into sulphuric and hydro-sulphuric acids—iodine, into hydriodic acid—oxalic, tartaric, gallic, succinic and benzoic acids into combinations with an alkali. Those which pass *unchanged* are the following: carbonate, chlorate, nitrate and sulphate of potash, hydro-sulphate, and hydro-cyanate of potash, protoxide of iron, borate of soda, muriate of barytes, silicate of potash, tartrate of nickel and potash. The principles of many colouring matters, such as indigo, gamboge, madder, logwood, beet-root, mulberries and cherries—several odoriferous principles, somewhat altered, such as the oil of turpentine, juniper berries, valerian, assafœtida, garlic, castor, saffron and opium.*

Still more recently, Orfila has detected the *presence of arsenic* in the urine of man, as well as of animals, poisoned by it. By him, *antimony* too has been found in the urine of persons who had been put upon the use of that substance. In one patient, who took twenty-four grains of tartrate of antimony in the course of twenty-four hours, for pneumonia, he obtained a sufficient quantity of the metal to exhibit it to the Academy of Medicine. In another patient, who took twelve grains in twenty hours, he detected the metal in the urine voided twelve hours after its administration. In experiments upon animals with the salts of copper, he discovered the presence of the metal in the urine.†

Of the Milk.—Let us now look at another of the secretions, and see what are the facts in relation to foreign substances getting into this. In animals, it is well known that the milk partakes of the character, as to taste, smell, and colour, of the peculiar vegetables upon which they have been feeding. Thus garlic, pepper-grass, and the like, impart their properties to the milk of cows, as well as the butter made from it.

By Chevallier, Henry, and Peligot, some interesting experiments were made on the milk of asses, to whom various substances were administered, and it was found that distinct traces of many remedial agents were detected in it. Of these, common salt was found in abundance. Sesquicarbonate of soda passed in great quantity into the milk, rendering it alkaline. Traces of sulphate of soda, when given in doses of about two ounces, were readily

* New York Medical and Physical Journal, vol. 5, p. 624.

† Johnson's Journal for Oct. 1840, p. 340.

detected. Iodide of potassium was readily identified, when administered in doses of a drachm and a half. Oxide of zinc, trisnitrate of bismuth, and sesquioxide were also found* By Mr. A. S. Taylor, of London, traces of *lead* were detected in the milk of a cow, poisoned by accidentally swallowing a quantity of carbonate of lead, which had been mixed for paint.†

In the human subject, *iodine* has in more than one instance been discovered in the milk. A woman, in Guy's Hospital, had been taking for a fortnight, three times a day, iodine with hydriodate of potash. On testing her milk with sulphuric acid and starch, iodine was detected.‡ According to Wallace, the milk of a nurse taking iodine, has not merely indicated its presence, but it has been found in the urine of the child at the breast.§

That certain medicines, too, taken by the mother affect the child through the medium of the milk, is a fact well established. This is very frequently observed by nurses with regard to cathartics.‖

By. M. Vallet, *iron* was found in the milk of a woman, under treatment with carbonate of iron. In women in health he did not find iron in the milk.¶

Opium sometimes, too, acts upon the child in this way. Barbier relates a case in which he saw an infant narcotized for several hours in consequence of having sucked the milk of a nurse, who had a short time before swallowed a large dose of laudanum for cramp in the stomach.** A similar case is related by Dr. E. D. Smith, on the authority of the late Prof. Barton, of Philadelphia.††

That the specific effects of *mercury* may be produced in the child through the milk of the nurse, is established by the best possible evidence, which is the cure of the venereal disease in the infant. Although it would not be safe in all cases, to trust exclusively to this mode of introducing mercury into the system of the child, yet the controlling influence of the remedy given in this way, has been noticed in too many cases to admit of any doubt.‡‡ In the Medical Essays and Observations of Edinburgh two cases are related, in which the yaws were cured in children by giving mercury to the mother.§§

Of the Saliva.—Iodine has been detected in the saliva of persons under its

* Johnson's Journal, vol. 37, p. 380.

† Johnson's Journal for July, 1841, p. 256.

‡ Johnson's Journal, vol. 37, p. 380.

§ London Lancet for March 26, 1836, p. 6.

‖ "The medicines which affect the child the least are olive oil, castor oil, confectio sennæ and compound extract of colocynth. The saline purges are apt to affect the child's bowels."—*Johnson's Journal*, vol. 36, p. 380.

¶ Journal of Pharmacy, vol. 10, p. 253.

** Traité élémentaire de Matière Médicale, par J. B. C. Barbier. Tome 2, p. 702.

†† Caldwell's Theses, vol. 1, p. 244.

‡‡ On this subject see Swediaur on Syphilis, p. 330. B. Bell on the Venereal, vol. 2, p. 263. Colles' Practical Observations on the Venereal Disease, p. 169. Hamilton on Mercury, p. 47. Ryan's Midwifery, p. 483.

§§ Vol. 6, p. 278.

use by Cantu,* and by Dr. A. T. Thomson, of London.† By Dr. O'Shaughnessy, it was found in the saliva of a dog that had been poisoned by it. The same fact is confirmed by Dr. Wallace.‡

That *lead* taken internally, makes its way into the saliva, appears to be now well established. Although I am not aware that the metal has been actually identified in this fluid, yet the peculiar effects produced by it upon the saliva and the gums are sufficient to prove its actual presence there —these are the bluish colour of the saliva, and a peculiar discoloration of the gums. That lead sometimes produces an increased flow of saliva, and renders it of a bluish colour, had been noticed by more than one observer, but the discoloration of the gums caused by it, was first noticed and described by Dr. Henry Burton, in a paper contained in the Transactions of the Royal Medical and Chirurgical Society of London, for 1840. According to him, "the edges of the gums attached to the neck of two or more teeth of either jaw, are distinctly bordered by a narrow leaden blue line, about the one-twentieth part of an inch in width, whilst the substance of the gum apparently retains its ordinary colour and condition." This discoloration is so peculiar, that when once seen, it may afterwards be recognized without any difficulty. It is very permanent, too, having continued for months and until after death. A few hours after death it appears more distinct than during life. Besides this, it is not an occasional, but a constant occurrence in persons under the influence of lead.§ Now that the bluish colour of the saliva and this blue line on the gums, depends upon the actual presence of the lead, in some shape or other, can hardly be questioned. Pereira explains it, by supposing that a sulphuret of lead is formed by the action of sulphuretted hydrogen, evolved by the lungs, on the lead contained in the salivary and buccal secretion. In confirmation of this opinion, he adds that he has seen "an alloy of mercury and silver, introduced into the hollow of a tooth, become coated in a few days with a black film of metallic sulphuret."‖

In connection with the subject of the absorption of lead, there is an interesting occurrence related by the learned Thunberg, which is not unworthy of being recorded. During the voyage to the Cape of Good Hope, about twenty of the officers and men were poisoned in consequence of some white lead being accidentally mixed with their food. He himself was severely affected, and he gives a detailed account of his symptoms. Besides the ordinary symptoms of colic, &c., he speaks particularly of the swelling of the gums, continued salivation, and on the tenth day after he was attacked, he speaks of lead as "perceived in his saliva."¶

* North American Medical and Surgical Journal, vol. 7, p. 432.

† Johnson's Journal, vol. 29, p. 215. ‡ London Lancet, N. S. vol. 7, p. 613.

§ For many interesting details in relation to this subject, see Transactions of the Royal Medical and Chirurgical Society of London, vol. 23, p. 63.

‖ Pereira's Materia Medica, vol. 1, p. 153, Am. ed.

¶ Travels in Europe, Africa and Asia, made between the years 1770 and 1779. By Charles Peter Thunberg, M. D., 3d. ed., Lond., vol. 1, p. 83.

Of the Perspiration.—By Dr. A. T. Thomson, *iodine* has been detected in the perspiration of those using it, and the same has been done by Cantu.*

That *sulphur* taken internally, passes off by the skin, cannot well be questioned. When continued for any length of time, the perspiration gives out a smell of sulphuretted hydrogen. Articles of gold and silver worn by the patients are blackened, and sometimes their linen is tinged yellow.†

That *mercury* passes off by the skin is proved by the blackening of the skin, which has been known to follow its use after the administration of sulphur. A case of this kind, quoted by Pereira, is related by Rigby, (*Lond. Med. Rep.*, for April, 1837.) In this case the sulphur and mercury are both thrown out by the skin, forming the black sulphuret of mercury on the surface.‡

Of the bones and soft solids.—That the bones of animals fed upon madder are coloured red has long been known, and what is curious is, while it thus tinges the bones, it does not affect in any way the soft solids. The oldest writer who notices this interesting property of madder appears to have been Lemnius, in his treatise, *De miraculis occultis naturæ.* He was a physician of Zealand, a country in which the madder has been cultivated from the earliest periods. His work was published in the year 1564.§ It did not, however, attract any attention until a much later period, about a century ago, when an English surgeon, by the name of Belchier, accidentally observed that the bones of some pork brought upon the table were red. On inquiry, he ascertained that it was occasioned by the animals feeding on the water mixed with bran in which cotton cloth was boiled, and which was coloured by the madder used in printing it. By subsequent experiments he convinced himself that the colouring of the bones was owing to the madder. In 1736, he communicated the discovery to the Royal Society of London, in a paper which was published in their Transactions.‖ Recent experiments not merely confirm the fact, of which indeed there is no doubt, but prove also that the bones are tinged by other substances.—Dr. Milnor, of Philadelphia, found that the bones of a cat fed for several days on *Prussian blue* and *indigo*, exhibited the blue colour "in a remarkable degree."¶ In a dog too, fed upon *indigo* for ten days, the bones, on dissection, were found to be "spotted in many places with the indigo tint."** He also found that a dog fed upon *madder and anotta* for twelve days had his bones of a light pink colour, which on boiling, assumed a dark reddish hue.†† Even the bones of the fœtus, have become coloured by feeding the parent animal on madder. To show this, some highly interesting experi-

* Christison on Poisons, p. 13.
† Dict. de Mat. Méd. Par Mérat et De Lens, tom. 4, p. 452.
‡ Pereira, vol. 2, p. 590.
§ Beckman's History of Inventions and Discoveries, vol. 3, p. 276.
‖ Philosophical Transactions, vol. 39, pp. 287, 299.
¶ Philadelphia Journal of Medical and Physical Sciences, vol. 4, p. 14.
** Ibid., vol. 4, p. 17.
†† Ibid., vol. 4, p. 16.

ments were made by Prof. Mussey, now of Cincinnati. He caused a sow to be fed daily during the last eight weeks of gestation, on madder. On the day the farrow was produced, several of the pigs were killed and their bones inspected, when every bone was found strongly tinged with red. In another experiment, a sow was fed for twenty days on madder—she was then bled to death, and half a dozen nearly full grown pigs found in the uterus—on examination, all the bones of the pigs were of a reddish colour. The bones of the sow too were dyed of a fine red, approaching scarlet.*

The bones of the Canada porcupine, during winter, are said to be of a greenish yellow colour, owing, as is supposed, to the bark of the pine on which the animal feeds in that season of the year.†

That *mercury* is deposited in the bones of those who have undergone a long course of mercurial medication, is an opinion which has been entertained, almost ever since that article was used for the cure of the venereal disease. By many, I am aware, this idea is ridiculed. Ridicule, however, is a poor substitute for argument. And unless we call in question the accuracy of all the facts reported on this subject, the occasional occurrence of it must be admitted.‡ That a long course of mercury does in some way or other affect the osseous system is certain. Thus, for example, the fact has been observed that the bones of those who have undergone such courses of mercury, never make such white or elegant skeletons as others.§ Dr. Monro too, in his anatomy, mentions mollities ossium as having succeeded a course of mercury.‖

That the *skin* becomes permanently affected by the internal use of *nitrate of silver*, is now established by so many cases, that no doubt can exist on the subject. This interesting fact appears to have been first noticed by Swediaur, who relates the case of a protestant clergyman, near Hamburgh, who took by the advice of an empiric, some nitrate of silver, for an obstruction of the liver. After continuing the use of it for some months, his skin began to change gradually, until at last it became almost black. This colour continued for several years and then began, as is stated, to diminish.¶ It was not, however, until the year 1815, that the fact was fairly brought before the notice of the profession, by Dr. Albers, a distinguished physician of Bremen, who gave an account of it in a paper which was published in the Medico-Chirurgical Transactions of London. Of one case which fell under his observation, he gives the following details: A woman aged thirty years,

* American Journal of Medical Sciences, vol. 5, p. 20.

† Pennant's Arctic Zoology, vol. 1, p. 126, as quoted by E. D. Smith. Caldwell's Theses, vol. 1, p. 254.

‡ For a detail of facts on this subject, accompanied with some judicious reasoning, I must refer to Christison on Poisons, p. 290.

§ Principles of Military Surgery. By John Hennen, M. D., &c., p. 397. Am. ed.

‖ Ibid. p. 397.

¶ La Medecine eclairée par les Sciences physiques, &c. Foureroy. Tom. 1, p. 342. Lond. Med. Chir. Trans., vol. 7, p. 292.

who was attacked with epileptic fits, was put upon the use of nitrate of silver, in the form of pills, night and morning. By the use of this remedy the disease was completely arrested, but without the knowledge of Dr. Albers, she continued the use of the pills for nearly three years and a half. Towards the end of the last year, a change of complexion became observable, and particularly in the face. "The tinge was at first bluish; it then grew gradually darker, till at last it became, as it remained afterwards, quite dark and almost black. The blue colour spread all over the body. It was most intense on the face, on the fore part of the neck, as far as the middle of the bosom, and on the hands and nails. The sclerotica was also discoloured." The blood appeared on examination, similar to that of a person in perfect health, and in every other respect she was perfectly well. Various remedies were used to remove the discoloration, such as sulphuric and nitric acids, chalybeates, baths, &c., but all to no purpose, and at the time when Dr. Albers gives the account of the case, it had remained in this state for ten years.* In the same paper three other cases are related, in which the same effect was produced in epileptic patients, who used this remedy. By Dr. Roget of London, another case of a similar kind is related. The subject was a lady twenty-five years of age who was attacked with epilepsy, and to whom the remedy was given for four or five months. What is curious in this case, the blackness did not show itself until some months after the discontinuance of the remedy. The tongue and fauces first became black as if stained with ink, and gradually the whole skin became affected. No symptom of the original disease returned.† After the lapse of twelve years, the discoloration remained unchanged.‡ About the same time, by Bertini, of Geneva, in a dissertation entitled "*De usu interno præparationum argenti*," three cases of a similar character are recorded. In all of these cases, the disease for which the remedy was prescribed was epilepsy.§ In 1818, Dr. Badeley published a case in which a young man was cured of epilepsy by the nitrate of silver, taken in doses of from a grain to a grain and a half, three times daily for a year and a half. In this case, besides the skin, the roof of the mouth, the inside of the cheeks, and back part of the tongue was dark. The tunica sclerotica was also discoloured.‖ By Dr. Vetch, a case is related of a lady, who after a long continued use of this article, became discoloured in the upper part of the body, while the colour of the lower was unchanged; and in both eyes, the iris, which was naturally of a black or deep brown, was changed to a light blue colour.¶ Dr. Paris gives the history of a case in which this discoloration was produced in a lady, who took large quantities of nitrate of silver, for a dyspeptic complaint.** Still more

* Medico-Chirurgical Transactions of London, vol. 7, p. 284.
† Ibid., vol. 7, p. 284.
‡ Cooke on Nervous Diseases, p. 397, Am. ed.
§ Medico-Chirurgical Transactions of London, vol. 7, p. 293.
‖ Ibid., vol. 9, p. 238.
¶ Cooke on Nervous Diseases, p. 397.
** Pharmacologia, p 296, Am. ed.

recently, M. Rayer, of Paris, has recorded four cases of this kind which fell under his observation.* By M. Lelut two cases are reported in which not merely the skin, but the mucous membrane of the stomach and intestines, presented the same appearance. One of these cases was that of a young man, twenty-eight years of age, who had taken nitrate of silver for thirteen months for epilepsy. A short time afterwards (in 1822) his skin began to blacken. In 1827 he died, and was then examined, and the following account is given of the appearances observed. "All the external integument was of a gray slate colour of moderate intensity. This hue, which was nearly the same in all parts of the skin, did not prevent the vascular colour of the cheeks from being distinguished. The edges of the lips, their internal surface, the inside of the cheeks, and both sides of the tongue, presented an exactly similar hue; the internal surface of the whole alimentary canal was of the same colour as the skin and the upper opening of the gastro-pulmonary membrane. In the stomach, this tint was extremely deep; it was not mixed with any violet coloured marblings, depending on vascular patches or striæ; it was uniform over the whole extent of the viscera. In both the small and great intestines it was a little clearer, but still very appreciable; it was uniform as in the stomach, and slight traces only of vascular ramifications were discovered in the whole extent of the alimentary canal."† According to M. Lelut, the seat of the discoloration is the chorion. He thinks the epidermis and the rete mucosum are not necessarily affected.

In addition to the foregoing, another case is related by Wedemeyer, of an epileptic, who was cured by nitrate of silver, but died afterwards of diseased liver and dropsy. His skin had previously acquired the bluish tint; on examination after death, all the internal parts were found similarly discoloured; and on chemical examination, metallic silver was found by M. Brandes, in the plexus choroides and pancreas.‡

I have been thus particular in detailing the foregoing cases of the effects of nitrate of silver, because I look upon them as furnishing one of the most striking and interesting of the proofs of the absorption of medicines. That the discoloration in these cases is owing to the deposition of the silver on the affected surface, cannot, I think, be questioned. In what state precisely, it is thus deposited, is not satisfactorily established, but that it does exist there in some form or other is certain, and that it must have got there by being absorbed and carried into the circulation is equally certain.§

* On Diseases of the Skin, p. 962.

† Rayer on Diseases of the Skin, p. 963.

‡ Brande's Journal of Science, new series, vol. 6, p. 430.

§ Prof. A. T. Thomson supposes that the nitrate of silver, after passing into the circulation undecomposed, is converted into the chloride when it gets to the skin. "The chloride, we know," says he, "acquires a gray, leaden colour, whenever it remains in contact with animal matter, and as it is insoluble, it is incapable of being reabsorbed, is

Besides the facts already detailed, the recent experiments of Orfila with *arsenic, tartar emetic*, and the *salts of copper*, furnish the most overwhelming evidence of the absorption of these articles, and of their subsequent appearance in the *solid viscera*, both of animals and of the human subject. In several cases, arsenic has been extracted by him after death, from the *liver* of persons poisoned by it, and in an aged female, who died fifteen hours after taking ten grains of tartar emetic, distinct traces of antimony were found in the *liver*, *kidneys*, and *spleen*.* *Copper* was found in the lungs, heart, liver, spleen, and kidneys of the animals to whom it was given. In a case of death by poisoning by arsenic, Mr. Taylor, of London, also detected it in the liver.†

I have thus, in a summary way, detailed a number of facts, from which the following conclusions may safely be drawn:

1. That both in man and in animals, foreign substances may and do get into the circulating fluids.

2. That among these, are several medicinal agents in ordinary use.

With so many positive proofs of the absorption of various articles, it is reasonable to infer, too, that when the range of experiments shall be sufficiently extended, and the processes for detecting substances shall have become sufficiently improved, we shall be able to establish the same in relation to a great number of agents concerning which, we have at present no certain evidence. In the mean time, it ought to be recollected, that the fact of our not being able to detect the presence of any article in the fluids, furnishes no certain proof that it does not actually exist in them. This is a point which has been argued with great clearness by Dr. Christison, in relation to poisons, and it holds with much greater force in its application to ordinary medicines. Among others, the two following reasons seem most conclusively to establish this. In the first place, the quantity of the article which enters the blood, may be too small to admit of detection, after being distributed throughout the body. Thus Sir Everard Home found, that a quarter of a grain of prussiate of potash could not be detected in two ounces of the serum of the blood. It required to be increased to a whole grain before the usual tests indicated its presence.‡ In the second place, many substances entering the blood may undergo such changes as to render their detection by chemical reagents impossible. Of this Dr. Christison gives a striking illustration. He injected into the femoral vein of a dog, eight grains and a half of oxalic acid, which caused death in thirty seconds, yet he could not

fixed in the rete mucosum, and a permanent stain is given to the skin. This effect, therefore, happens whenever a more than usual quantity of muriates is separated by the cuticular capillaries."—*Elements of Mat. Med. and Therapeutics*, vol. 1, p. 714. London.

* Medico-Chirurg. Journal for 1840, p. 43. Boston Med. and Surgical Journal for 1840, p. 118.

† Guy's Hospital Reports, vol. 7, p. 341.

‡ Philosophical Transactions of London for 1808, p. 53.

detect it in the blood of the iliac vein and vena cava collected immediately after death.* These considerations unquestionably prove that substances may exist in the blood and yet not be cognizable by the ordinary tests.

That certain medicinal substances are taken into the circulation is then proved beyond question. This being so, another point remains to be settled, and this relates to the precise mode in which their effects are finally produced. On this there are two different opinions. By some, it is supposed, that the medicine after being introduced into the current of the circulation, is carried to different parts of the system and produces its effects by actual contact with the parts or organs in which its agency is developed. Others again have conjectured that the medicine mingled with the blood, merely makes an impression upon the nerves of the inner membrane of the blood-vessels, and that this impression is sympathetically transmitted to distant parts. Without denying that some may act in this latter way, the probability is that the former is the more general mode of operation.

In conclusion, the propositions, which, in the present state of our knowledge of the action of medicines, appear to me to be entirely defensible, are the following:

1. That medicines differ in the manner in which their remote effects are produced.

2. That some produce their remote effects by sympathy, or through the medium of the nerves.

3. That others produce their remote effects in consequence of being absorbed into the circulation.

4. That those which are absorbed, produce their effects in different ways —some, probably, by making an impression on the nerves of the inner membrane of the blood-vessels, and having this impression propagated to other parts sympathetically—some, by being carried through the circulation to distant parts and acting on them by actual contact,—while others again, are mingled with the blood, pervade every portion of the system, and thus in a greater or less degree, modify the condition, not merely of the fluids, but of the very solids of the body.

Each of these propositions might furnish the basis for much comment, and many inferences of practical importance. The length to which this paper has already extended itself, however, forbids my entering upon them at present.

* On Poisons, p. 14.